REMARKS

The present claims are drawn to purified polypeptides related to SEQ ID NO:2, a polypeptide described in the present application as a glutamine synthetase-like (GS-like) protein. Claims 5-17 have been cancelled. Claim 4 has been amended to create an independent claim. Claim 18 has been added. This new claim finds support in the specification, for example, at line 30 of page 15. No new matter has been added.

Double Patenting

The Examiner provisionally rejected claims 1-4 under the judicially created doctrine of obviousness type double patenting as unpatentable over claims 1-4 of co-pending U.S. Serial No. 10/446,520. Applicants will address this rejection if it is still present when they are notified that the application includes allowable claims.

Rejections Under 35 U.S.C. §101 (utility) and 35 U.S.C. §112, first paragraph (enablement)

The Examiner rejected claims 1-4 under 35 U.S.C. §101 as lacking utility. In a related rejection the Examiner rejected claims 1-4 under 35 U.S.C. §112, first paragraph as not enabled because, according to the Examiner, "the claimed invention is not supported by either a credible asserted utility or a well established utility". The Examiner also argued that claims 1-3 are not enabled because the specification does not teach one of ordinary skill in the art how to make and use polypeptides that are functional and have the specified degree of identity to SEQ ID NO:2.

The Examiner argued that the claims lack utility because it is not credible that polypeptide having the sequence of SEQ ID NO:2 is a glutamine-synthetase and because all of the disclosed utilities for the claimed polypeptides depend on SEQ ID NO:2 being a glutamine synthetase or are utilities that would apply to every member of a general class of materials, i.e., all proteins.

First, Applicants point out that SEQ ID NO:2 is proposed to be glutamine synthetase-like polypeptide, not simply a glutamine synthetase. As explained in the specification, for example at pages 16-18, glutamine synthetase-like polypeptide of SEQ ID NO:2 is expected to be useful as a

target for the identification of nematicidal compounds because is more closely resembles bacterial glutamine synthetases than mammalian or plant glutamine synthetases and because glutamine synthetases are thought to provide an essential function. Thus, inhibitors of SEQ ID NO:2 function could inhibit, for example, an *M. incognita* glutamine synthetase-like protein without interfering with the function of mammalian or plant enzymes. This specificity means that the inhibitors could be safe and effective nematicides.

Regarding whether it is reasonable to conclude that SEQ ID NO:2 is a GS-like polypeptide, the Examiner argues that Applicants' assertion that SEQ ID NO:2 is a GS-like polypeptide is based on the fact that SEQ ID NO:2 is 36% identical to a protein identified as *M. tuberculosis* glutamine synthetase and that this fact does not amount to a credible basis for concluding that SEQ ID NO:2 is a GS-like polypeptide.

As explained in the accompanying Declaration of Andrew P. Kloeck (**Exhibit A**), Applicants' assertion that SEQ ID NO:2 is a GS-like polypeptide is based, in part, on Pfam analysis. As the Examiner is likely aware and as Dr. Kloeck explains in his declaration, Pfam is a curated database of protein domain families and related analytical tools. The database and the analytical tools associated with the database are designed to provide a more accurate assessment of protein function than can be achieved by simple pair-wise sequence comparisons such as BLAST analysis. Pfam is available on the Internet at www.sanger.ac.uk/Software/Pfam/ and is described in Bateman et al. 2002 *Nucleic Acids Research* 30:276.

As Dr. Kloeck explains in his declaration, SEQ ID NO:2 was initially identified as a GS-like polypeptide protein based, in part, on Pfam analysis. This analysis, which involves comparing a test sequence (e.g., SEQ ID NO:2), to Hidden Markov Model (HMM) descriptions of more than 1800 protein domain families, each of which has multiple representative members. Pfam analysis assigns an S-score to each comparison between the test protein and a HMM of the protein domain family. This S-score is a measure of the relatedness test protein to the particular protein domain family. The S-score has an associated "e-value". The e-value is a measure of the odds that the particular S-score for the test protein (or an even better S-score) could arise by chance. Put another way, the e-value is the number of hits that would be expected to have a

score equal or better than this S-score by chance alone. Thus, the lower the e-value, the lower the likelihood the match between the test protein and the protein domain family is a chance match and the greater the likelihood that the test protein is a member of the protein domain family. Furthermore, the manual curators of individual Pfam protein models set a score threshold called the "gathering threshold" (GA cutoff) which is considered to be trustworthy cutoff above which effectively zero false positives get through.

As Dr. Kloeck explains in his declaration, when the *M. tuberculosis* glutamine synthetase gene glnA4 (GenBank® Accession No. F70885) is subjected to Pfam analysis, the domain model sequence with the best e-value (i.e., lowest) is the glutamine synthetase domain model sequence. Pfam analysis assigns an e-value of $4.2e^{-89}$ to this comparison. As Dr. Kloeck explains, this value indicates that the match is highly unlikely to occur by chance. As Dr. Kloeck also explains in his declaration, Pfam analysis of SEQ ID NO:2 revealed that the domain model sequence with the best e-value (i.e., lowest) is the glutamine synthetase domain model sequence. Furthermore this is the only domain match above the gathering threshold. As Dr. Kloeck explains, this sequence comparison has an e-value of $1.7e^{-77}$ indicating that a match this good is highly unlikely to occur by chance. This analysis strongly supports the conclusion that SEQ ID NO:2 is a GS-like polypeptide. Finally, the Pfam analysis indicated that the glutamine synthetase domain extends from amino acid 115 to 375 of SEQ ID NO:2. Moreover, as Dr. Kloeck explains, the fact that the vast majority of the more than 30 proteins in the GenBank® database having the greatest similarity to SEQ ID NO:2 by BLAST analysis are identified as glutamine synthetases also supports the conclusion that SEQ ID NO:2 is a GS-like polypeptide.

Based on the forgoing, one skilled in the art would find Applicants' conclusion that SEQ ID NO:2 is a GS-like polypeptide to be credible.

Rejections Under 35 U.S.C. §112, first paragraph (written description)

The Examiner rejected claims 1-3 under 35 U.S.C. §112, first paragraph as failing to meet the written description requirement.

In *Regents of the University of California v. Eli Lilly & Co.*, the Court of Appeals for Federal Circuit held that an adequate written description of genetic material "requires a precise definition, such as by structure, formula, chemical name, or physical properties." 119 F.3d at 1563. The presently claimed nucleic acid molecules are defined by sequence or by sequence combined with function. Thus, the present claims meet the written description requirement as articulated by the court in *Eli Lilly*.

CONCLUSION

Enclosed is a Petition for Extension of Time with the appropriate fee. Please apply any other charges or credits to deposit account 06-1050.

Respectfully submitted,

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